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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/863,179	05/23/2001	Matthew J. During	102182-12	9640

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NUTTER MCCLENNEN & FISH LLP
WORLD TRADE CENTER WEST
155 SEAPORT BOULEVARD
BOSTON, MA 02210-2604

EXAMINER
FALK, ANNE MARIE

ART UNIT	PAPER NUMBER
1632	13

DATE MAILED: 09/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

File

Office Action Summary	Application No.	Applicant(s)	
	09/863,179	DURING ET AL.	
	Examiner	Art Unit	
	Anne-Marie Falk, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10, 12-31* is/are pending in the application.

4a) Of the above claim(s) *20-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,12-19 and 26-29* is/are rejected.

7)☒ Claim(s) *30 and 31* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 June 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The amendment filed June 30, 2003 (Paper No. 12) has been entered. Claim 12 has been amended. Claim 11 has been cancelled. Claims 26-31 have been newly added.

Accordingly, Claims 1-10 and 12-31 are pending in the instant application.

Claims 20-25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention. Applicant timely traversed the restriction requirement in Paper No. 10.

Accordingly, Claims 1-10, 12-19, and 26-31 are examined herein.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 1-10 and 12-19 stand rejected and Claims 26-29 are rejected under 35 U.S.C. 112, first paragraph, for reasons of record advanced on pages 4-8 of the Office Action of Paper No.11 (mailed 3/27/03), because the specification, while being enabling for a method of treating Parkinson's disease by administering to the subthalamic nucleus (STN) or the substantia nigra (SN) an rAAV vector comprising a nucleotide sequence encoding glutamic acid decarboxylase (GAD), wherein a symptom of Parkinson's disease is ameliorated, does not reasonably provide enablement for the use of any type of vector for the treatment of Parkinson's disease, nor for any target tissue other than the STN and SN. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicants arguments are partially persuasive. Thus, the scope of enablement has been expanded to include administration of the vector to the substantia nigra (SN).

At pages 3-11 of the response, Applicants argue that the art was replete with teachings that gene therapy was recognized as a realistic alternative treatment for neurodegenerative diseases such as Parkinson's disease. Applicants further argue that the articles they cite demonstrate that a number of different vectors had successfully been used to deliver therapeutic genes to different regions of the brain. However, Applicants are not claiming gene delivery of GAD to different regions of the brain. Rather, the claims require a sufficient level of gene expression within the appropriate location to provide amelioration of a symptom of Parkinson's disease.

At pages 11-13 of the response, Applicants argue that the references of Levy et al. (2001), Levy et al. (2002), Dostrovsky et al. (2000), and Pahapill et al. (1999) show that one of skill in the art would know which regions of the brain to target to treat a neurodegenerative disease. However, while one of skill in the art can identify a target region to which gene transfer is desired, identification of a target region is not sufficient to allow one of skill to provide sufficient expression of the desired gene within that location. As discussed in the previous Office Action successful treatment is dependent on the type of vector used, the tissue being targeted (i.e., obtaining expression of the gene within the target tissue), and the route of administration. These parameters must be addressed on a case by case basis.

At pages 13-16 of the response, Applicants argue that, with the knowledge available in the art combined with the guidance in the specification, the skilled artisan could readily deliver a vector carrying the GAD gene to a region of the brain other than the subthalamic nucleus. Again, while a variety of regions of the brain are clearly accessible for the purpose of gene delivery, the claims require much more than simply achieving gene delivery. Applicants are not claiming gene delivery, but rather are claiming treatment of Parkinson's disease which, in addition to gene delivery, also requires a sufficient level of gene expression within the appropriate location to effect the desired therapy. In view of Applicants'

arguments and evidence, the Examiner agrees that one of skill in the art would have a reasonable expectation of success in extrapolating the claimed method to include administration of a GAD AAV vector to the substantia nigra.

At pages 16-17 of the response, Applicants argue that their gene therapy procedure has been approved by the FDA. An appropriate scope of enablement has been indicated. Thus, the present rejection does not conflict with the action taken by the FDA.

At pages 17-20 of the response, Applicants argue that the references cited in the enablement rejection are dated. Applicants emphasize that gene therapy is an evolving field. Applicants point to three of the references that were published in 1995 (Miller et al., Crystal, and Orkin & Motulsky). The effective filing date of this application is May 23, 2000. Applicants seem to be arguing that the field of gene therapy as a whole advanced so rapidly in the five years from 1995 to 2000 such that the tools available would render therapeutic protocols relatively routine. However, the gene therapy art as a whole clearly demonstrates that even in the year 2000, despite intensive effort in every aspect of gene therapy, success in the field was quite limited. Furthermore, Rubanyi et al. (2001) was published after the effective filing date of this application and reflects essentially the same opinion of those stated in the other references cited regarding the technical barriers and very limited clinical efficacy. The quotes that Applicants refer to describing the optimism in the field of gene therapy is not indicative of enablement at present, but rather suggest that continued effort should result in successful protocols at some time in the future. However, future potential is not sufficient to demonstrate the need for only routine experimentation rather than undue experimentation, given that the art as a whole demonstrates that intensive effort has met with limited success.

Conclusion

No claims are allowable.

Claims 30 and 31 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

This application contains claims 20-25 drawn to an invention nonelected with traverse in Paper No. 10. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk whose telephone number is (703) 306-9155. The examiner can normally be reached Monday through Thursday and alternate Fridays from 10:00 AM to 7:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst, William Phillips, whose telephone number is (703) 305-3388.

Anne-Marie Falk, Ph.D.

Anne-Marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER